REMARKS

Applicants thank the Examiner for the personal interview of July 23, 2008 where the rejections were discussed. However, Applicants have not yet received the Interview Summary. Accordingly, Applicants respectfully request a copy of the Interview Summary.

After entry of this amendment, claims 1, 3-7, 39, and 44-46 are pending. Claims 2, 8-38, 40-43, and 47-48 are cancelled without prejudice or disclaimer. Claims 1 and 46 have been amended without disclaimer or prejudice. Support for the amendment is found *inter alia* in the original claims and in the specification, for example, at page page 14, lines 36-40, and at page 18, lines 18-23. No new matter has been added.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 3-7, 39, and 44-48 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement and for lack of an enabling disclosure. Applicants respectfully disagree and traverse the rejections in view of the present amendments. Nonetheless, in order to expedite prosecution, claims 47 and 48 are cancelled without disclaimer or prejudice; accordingly, the rejections as to these claims are rendered moot.

Written Description Rejection

The Examiner alleges that the specification does not disclose a correlation between structure and function and that there is no known disclosed protein having antifungal activity except for SEQ ID NO: 2 or 4. Applicants disagree with the Examiner's interpretation of the specification and conclusions.

Initially, the claimed subject matter relates to a **method** for generating or increasing the resistance against the phylum Oomyceta by expressing a transgenic Rpi-blb2 protein encoding nucleic acid mole cule in a plant. As set forth in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991), the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to one skilled in the art that the inventor had possession of the claimed subject matter at the time of

filing. According to the "Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement," at page A-6, 3rd column of the "Written Description Training Materials" (" Guidelines," March 25, 2008 revision), possession of an invention can be shown "in a variety of ways, including description of an actual reduction to practice." The present application describes an actual reduction to practice of the claimed method in Example 12. Thus, possession of the claimed method is shown, and the rejection should be withdrawn.

Moreover, the specification provides for six actual sequences related to the claimed nucleic acid, *i.e.* four nucleotides sequences SEQ ID NOs: 1, 3, 5, and 6, which encode the sequence of SEQ ID NO: 2 or SEQ ID NO: 4. Because the genetic code and its redundancies were known in the art at the time of filing, the disclosure of SEQ ID NO: 2 and SEQ ID NO: 4, combined with the pre-existing knowledge in the art, would have put one in possession of the genus of nucleic acids that encodes SEQ ID NO: 2 and SEQ ID NO: 4. With the aid of a computer, one skilled in the art could have identified all of the nucleic acids that encode a polypeptide with at least 95% homology with SEQ ID NO: 2 and SEQ ID NO: 4. Thus, one of ordinary skill in the art would conclude that Applicants were in possession of the claimed genus at the time the application was filed.

Furthermore, as described in the specification at page 17, lines 1-7, natural variations (*e.g.* DNA sequence polymorphisms) can lead to alterations in the amino acid sequences of the Rpi-blb2 sequences within a population, bringing about a variation of 1-5% in the nucleotide sequence of the Rpi-blb2 gene without altering the functional activity of the Rpi-blb2. Accordingly, the claim scope created by the recitation of at least 95% identity with SEQ ID NO: 2 or SEQ ID NO: 4 includes the expected range of natural polymorphic variants, which should certainly within the scope of the invention.

Additionally, the specification discloses conserved structures of the Rpi-blb2 sequences. As provided in the specification at page 92, lines 26-36, and Figure 14, conserved domains of the Rpi-blb2 proteins include LZ, NBS, and LRR domains, thus providing a correlation between structure and function:

> Several ***functional motifs present in R genes of the NBS-LRR class of plant R genes*** are apparent in the encoded protein. As illustrated in Figure 14, the Rpi-blb2 protein belongs to the leucine zipper (LZ) subset of NBS-LRR resistance proteins. The N-terminal half of the Rpi-blb2 protein contains a potential LZ region between amino acids 413 and 434 and ***six conserved motifs indicative of a nucleotide-binding site*** (van der Biezen and Jones, 1998). The C-terminal half of Rpi-blb comprises ***a series of 15 irregular LRRs*** that can be aligned according to the consensus sequence hxxhxxLxxLxLxxC/N/Sx(x)LxxLPxx ***observed in other cytoplasmic R proteins***, whereby h can be L, I, M, V or F, and x any amino acid residue (Jones and Jones, 1997). (Specification, page 92, lines 26-36; emphasis added).

Additionally, as discussed in the specification at pages 21-22, it is recognized in the art that at least NBS and LRR domains are common to genes associated with pathogen resistance. Contrary to the Examiner's characterization of *Ex parte Sun*, the specification does provide for conserved structures common to members of the claimed genus of Rpi-blb2 proteins, which further satisfies the written description requirement. The description of recognized domains common to members of the claimed genus does provide sufficient description for a structure/function relationship and should be considered adequately described based on Example 11B of the revised Written Description Guidelines of March 25, 2008 and also *Ex parte Sun*.

The specification therefore not only discloses a representative number of species by actual sequence but additionally discloses a structure/function relationship. Thus the specification provides adequate written description for the present claims under both alternatives of the *Lilly* standard. See *Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) (holding that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs defined by nucleotide sequence . . . or of a recitation of structural features common to members of the genus.") (emphasis added). Reconsideration and withdrawal of the rejection is respectfully requested.

In response to Applicants comments regarding the rejection based on hybridization language being unclear, the Examiners argues that the state-of the-art allegedly teaches that isolating DNA fragments using stringent conditions does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe, citing to Fourgoux-Nicol *et al.* for support. The Examiner further contends that Fourgoux-Nicol *et al.*

exhibits less than 50% sequence identity with the probe to which the fragment hybridize. The Examiner concludes that it would require undue experimentation to generate and verify variants of SEQ ID NO: 1, 3, 5, and 6 and still have anti-Oomycetes activity. Applicants strongly disagree with the characterization of the reference and the standard used by the Examiner. Whether or not undue experimentation would be required is irrelevant to determining compliance with the written description requirement. Furthermore, Fourgoux-Nicol *et al.* additionally discloses that when using M3 as a probe to isolate the corresponding gene, "[c]omparison of the M3 cDNA sequence with the sequence of the shortest ORF of the genomic clone revealed 1 difference out of 293 bp of the aligned coding sequence and 7 differences out of the 203 bp of the aligned 3'-downstream region." (see Fourgoux-Nicol *et al.*, p. 863, right column). Differences of 1 out of 293 or 7 out of 203 are far from the 50% asserted by the Examiner. A more applicable teaching than the identity of the probe to the fragment hybridized is that the expression pattern of both cDNAs, M3 and M3.21, appeared to be identical (see Fourgoux-Nicol *et al.*, p. 863, left column, second full paragraph). Thus contrary to the Examiner's assertion, even with the alleged low identity asserted by the Examiner, Fourgoux-Nicol *et al.* does teach how to generate variants having the same activity and verify the activity of the variants. Nonetheless, in order to expedite prosecution, claim 48 is cancelled without disclaimer or prejudice; accordingly, the rejection regarding hybridization is rendered moot.

Enablement Rejections

The Examiner rejects the claims for lack of enablement, alleging that the specification enables only the use of the nucleic acid molecules encoding the sequence of SEQ ID NO: 2 or 4, but not any variants thereof. Applicants respectfully disagree. Nonetheless in order to expedite prosecution, the claims have been amended without prejudice or disclaimer. In light of the amendments, the rejection is believed to be rendered moot. Reconsideration and withdrawal of the rejections is respectfully requested in light of the amendments and the following remarks.

The Examiner contends that the specification does not describe conserved structures that are essential to its functional activity, and that without such a correlation, a person skilled in the art would not know which residues can be modified. The Examiner supports this argument by discussing a polypeptide having 82% identity; however, the claims as previously amended did

not recite 82%, but rather 90%. The Examiner appears not to have considered the claim amendments presented with the last response. Thus the arguments presented by the Examiner are not relevant to the previously amended claims reciting 90% identity or the present claims which recite 95% identity. Applicants respectfully request that the Examiner consider the claims as amended.

Moreover the standard for determining enablement is not whether or not the specification describes a correlation between conserved structure and function. Rather the standard for enablement is "to teach those of ordinary skill how to make and use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 & n. 23 (Fed. Cir. 1991), *quoted in Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1374 (Fed. Cir. 1999). Some experimentation, even a considerable amount, is not "undue" if, e.g., it is merely routine, or if the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. *See In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

As previously explained, the specification provides detailed description including working examples on how to clone Rpi-blb2 proteins and how to carry out the claimed method. (see Amendment And Reply Under 37 CFR §1.111 dated October 24, 2007). Furthermore, as explained above, the specification discloses conserved regions of Rpi-blb2 (Figure 14 and page 92, lines 26-36), within which one skill in the art would know to avoid any substitutions or modification. In view of the detailed description, guidance, working examples, and high level of skill, the specification enables the full scope of the claim without undue experimentation. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine").

The Examiner further states that he disagrees that screening and testing for homologs and variants would be routine because of the alleged lack of description of conserved structures essential for function. Contrary to the Examiner's assertion, as explained above, the specification does describe recognized domains common to members of the claimed genus. Consistent with the holdings of the Board of Patent Appeals and Interferences in *Ex parte Sun* and *Ex parte Kubin* where compliance with the written description and enablement requirements

were found with an 80% identity, the present specification should likewise be found enabled. Moreover, the Examiner did not respond to Applicants' previous arguments regarding these decisions and thus has not explained why the specification would not be enabling under the standard as set forth in these decisions.

Additionally, the Examiner contends that the specification only teaches how to practice the invention by expressing the claimed protein as a transgene in transgenic plants. The Examiner appears not to have considered the amendments presented in the previous response, where claim 1 recites: "... increasing the activity of a Rpi-blb2 protein in the plant or a tissue, organ or cell of the plant or a part thereof by expressing a transgenic Rpi-blb2 protein encoding nucleic acid molecule ...." Accordingly, the rejection is believed to be rendered moot.

The Examiner further alleges that the specification is silent as to how to use other methods to increase the activity of Rpi-blb2 protein. Applicants strongly disagree. First, a patent need not disclose what is well known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). The steps recited in claim 6 refer to general methods for increasing the activity of a protein which are well known in the art (see also specification, for example, at page 28 line 10 through page 29 line 38). Such methods are useful for increasing the activity of Rpi-blb2 as well as other resistance proteins. Moreover, contrary to the Examiner's assertion, the specification does describe various methods to increase protein activity (see specification, page 28 line 10 through page 29 line 38). For example, the specification describes inducing factors such as inducible promoters at page 38, lines 27-28, and at pages 40-41 c) and d); transcription factors at page 35, lines 4-5; increasing the copy number of the resistance protein encoding gene in Example 12 at page 91, lines 30-35; etc.

Furthermore, in light of the comments already of record and those above, Applicant's attorney respectfully reminds the Examiner that the representations in the specification as to the manner of making and using the claimed invention must be taken as in compliance with the first paragraph of 35 U.S.C. §112, unless there is objective evidence or scientifically based reasoning inconsistent with the specification. *See In re Marzocchii and Horton*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). "It is the Patent Office's burden to present evidence that there is some reason

to dispute the enablement provided in the specification. Unsupported speculation or conjecture on that the invention "might not work" will not support a rejection based on 35 U.S.C. §112, first paragraph." *Id.*

As provided herein, Applicants respectfully submit that the art and the specification provide ample guidance and predictability for the present claims and the Examiner has not presented the evidence necessary to dispute the enablement provided in the instant specification. Accordingly, the Patent Office has not met its burden and reconsideration and withdrawal of the enablement rejections is requested.

CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Accompanying this response is a petition for a one-month extension of time to and including February 2, 2009 pursuant to 37 CFR § 1.7(a) with the required fee authorization. No further fee is believed due. However, if an additional fee is due, the Director is authorized to charge our Deposit Account No. 03-2775, under Order No. 13477-00002-US from which the undersigned is authorized to draw.

Respectfully submitted,

By 

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